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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MCINTOSH III, TRAVISS C	

ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/609,298	LACOLLA ET AL.	
	Examiner	Art Unit	
	TRAVISS C. MCINTOSH III	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11,17-25,43-55 and 62-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11,17-25,43-55 and 62-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The Amendment filed 2/25/2008 has been received, entered into the record, and carefully considered. The following information provided in the amendment affects the instant application by:

Claim 11 has been amended.

Claims 1-10, 12-16, 26-42, and 56-61 have been canceled.

Remarks drawn to rejections of Office Action mailed 8/24/2007 include:

Double Patenting Rejections: some of which have been maintained and some of which have been withdrawn for reasons set forth below.

An action on the merits of claims 11, 17-25, 43-55, and 62-71 is contained herein below. The text of those sections of Title 35, US Code which are not included in this action can be found in a prior Office action.

Double Patenting

The rejection of claims 11, 17-25, 43-55, and 62-71 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-32 of U.S. Patent No. 6,812,219 is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to treating Flaviviridae infections in a host using 2'-methyl-pyrimidine nucleosides. It is noted that the

instant application requires a 3'-amino acid moiety, and the '219 patent comprises H or phosphate at the 3' and 5 positions, however, the '219 patents claims are also drawn to "or prodrugs thereof". Likewise, US 6,875,751 teaches that 3'-amino acid groups are cleavable esters which act as prodrug moieties for nucleotide therapeutics (see column 3, line 35 to column 4 line 45). As such, the amino acids instantly claimed are art known prodrugs. Obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979).*** Prodrug esters are well known in the art, as are amino acid prodrug esters as evidenced by US 6,875,751, as such, absent unexpected results, the examiner believes it would be obvious to make 3'-amino-acid prodrug esters of the '219 patent's compounds.

Applicants arguments filed 2/25/08 have been considered but are not persuasive. Applicants argue that the instant claims are drawn to treating HCV and the '219 patent is drawn to treating flavivirus and pestivirus infections. However, it is noted that the claims as filed in the instant application were drawn to treating a Flaviviridae virus, which is a family that encompasses flavivirus, pestivirus, and HCV. As such, this is seen to render obvious treating any member of the Flaviviridae family with the same therapy. Moreover, applicants also argue that there is nothing in the art showing the instantly claimed 3'-prodrugs. The examiner has cited the 6,875,751 patent above to show this feature. Applicants also argue that example 36 of the instant application provides unexpected results with respect to bioavailability and anti-viral activity, thus

rebutting any prima facia case of obviousness. However, it is noted that example 36 is not seen to compare the valine-esters with the non-valine compounds, but rather show that the valine esters produce HCV activity, which would be expected. There are no results in example 36 comparing the claimed compounds to the non-prodrug compounds.

The rejection of claims 11, 17-25, 43-55, and 62-71 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-27 of U.S. Patent No. 6,914,054 is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to treating HCV infections in a host using 2'-methyl-pyrimidine nucleoside. It is noted that the instant application requires compounds which comprise a 3'-amino acid ester prodrug moiety, and the '054 patent comprises H or phosphate at the 3' and 5 positions, however, the '054 patents claims are also drawn to "or prodrugs thereof". Likewise, US 6,875,751 teaches that 3'-amino acid groups are cleavable esters which act as prodrug moieties for nucleotide therapeutics (see column 3, line 35 to column 4 line 45). As such, the amino acids instantly claimed are art known prodrugs. Obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979).*** Prodrug esters are well known in

the art, as are amino acid prodrug esters as evidenced by US 6,875,751, as such, absent unexpected results, the examiner believes it would be obvious to make 3'-amino-acid prodrug esters of the '054 patent's compounds.

Applicants argue that the '054 patent is drawn to treating flavivirus and pestivirus infections, and the instant application to HCV, however, the claims of both application are drawn to treating HCV, not flavivirus and pestivirus infections. Applicants also argue that there is nothing in the art showing the instantly claimed 3'-prodrugs. The examiner has cited the 6,875,751 patent above to show this feature. Applicants also argue that example 36 of the instant application provides unexpected results with respect to bioavailability and anti-viral activity, thus rebutting any prima facia case of obviousness. However, it is noted that example 36 is not seen to compare the valine-esters with the non-valine compounds, but rather show that the valine esters produce HCV activity, which would be expected. There are no results in example 36 comparing the claimed compounds to the non-prodrug compounds.

The rejection of claims 11, 17-25, 43-55, and 62-71 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 and 8-18 of US Patent No. 7,105,493 is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of treating Flaviviridae infections by administering pyrimidine 2'-methyl-ribofuranosyl nucleosides, or prodrug or esters thereof. It is noted that the instant application requires compounds which comprise a 3'-amino acid ester prodrug moiety, and the '493 patent comprises H or phosphate at the 3' and 5' positions, however, the '493 patents claims are also drawn to "or

prodrugs thereof". Likewise, US 6,875,751 teaches that 3'-amino acid groups are cleavable esters which act as prodrug moieties for nucleotide therapeutics (see column 3, line 35 to column 4 line 45). As such, the amino acids instantly claimed are art known prodrugs. Obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979).*** Prodrug esters are well known in the art, as are amino acid prodrug esters as evidenced by US 6,875,751, as such, absent unexpected results, the examiner believes it would be obvious to make 3'-amino-acid prodrug esters of the '493 patent's compounds.

Applicants arguments filed 2/25/08 have been considered but are not persuasive. Applicants argue that the instant claims are drawn to treating HCV and the '493 patent is drawn to treating flavivirus and pestivirus infections. However, it is noted that the claims as filed in the instant application were drawn to treating a Flaviviridae virus, which is a family that encompasses flavivirus, pestivirus, and HCV. As such, this is seen to render obvious treating any member of the Flaviviridae family with the same therapy. Moreover, applicants also argue that there is nothing in the art showing the instantly claimed 3'-prodrugs. The examiner has cited the 6,875,751 patent above to show this feature. Applicants also argue that example 36 of the instant application provides unexpected results with respect to bioavailability and anti-viral activity, thus rebutting any prima facia case of obviousness. However, it is noted that example 36 is not seen to compare the valine-esters with the non-valine compounds, but rather show that the valine

esters produce HCV activity, which would be expected. There are no results in example 36 comparing the claimed compounds to the non-prodrug compounds.

The provisional rejection of claims 11, 17-25, 43-55, and 62-71 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 130-131 and 137-149 of copending Application No. 10/602,691 is maintained for reasons of record. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim methods of treating HCV using overlapping 2'-methyl pyrimidine nucleosides. It is obvious that the instant application and the '691 application are substantially overlapping.

Applicants argue that the '691 application does not recite the instantly required 3'-amino acid substitutions and without articulating a reason why this modification would occur, no obviousness can be made. The examiner notes that US 6,875,751 teaches that 3'-amino acid groups are cleavable esters which act as prodrug moieties for nucleotide therapeutics (see column 3, line 35 to column 4 line 45). As such, the amino acids instantly claimed are art known prodrugs. Obviousness based on similarity of structure and function entails motivation to make claimed compound in the expectation that compounds similar in structure will have similar properties. Where the prior art compounds essentially bracket the claimed compounds and are known to be effective as well known pesticides, for example, one of ordinary skill in the art would be motivated to make the claimed compounds in searching for new pesticides. See ***In re Payne, 606 F.2d 303, 203 USPQ 245, 254-55 (CCPA 1979)***

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The rejection of claims 11, 17-25, 43-55, and 62-71 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2-3, 8-17, and 19-66 of copending Application No. 11/005,443. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim methods of treating flavivirus infections using overlapping 2'-methyl pyrimidine nucleosides which have 3'-amino acid prodrug moieties. It would be obvious to one of skill in the art that these applications are claiming substantially overlapping subject matter.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 11, 17-25, 43-55, and 62-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 8-17, 19-21, 25, 29-37, 39, and 52 of copending Application No. 11/005,440. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications claim methods of treating flavivirus infections or HCV using overlapping 2'-alkyl pyrimidine nucleosides which comprise 3'-amino acid prodrug moieties.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 11, 17-25, 43-55, and 62-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2, 3, 8-17 and 19-57 of copending Application No. 11/005,446. Applicants are correct in their assertion that the examiner typed in the wrong application number for this rejection, the examiner previously typed "11/005,449" and it was intended "11/005,446". Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of treating HCV by administering pyrimidine 2'-methyl-ribofuranosyl nucleosides. It is obvious that the instant application and the '446 application are substantially overlapping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 11, 17-25, 43-55, and 62-71 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 19-36, 39-42, and 45 of copending US Application 11/516,928. Although the conflicting claims are not identical, they are not patentably distinct from each other because both applications are drawn to methods of treating Flaviviridae infections by administering 3'-amino acid prodrugs of pyrimidine 2'-methyl-ribofuranosyl nucleosides. It is obvious that the instant application and the '928 application are substantially overlapping.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Traviss C. McIntosh whose telephone number is 571-272-0657. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Traviss C McIntosh III/

Examiner, Art Unit 1623

July 7, 2008